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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,711	04/03/2000	FRANCE ALLARD	P04334USO	2785

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/446,711	Applicant(s) ALLARD ET AL.	
	Examiner Cynthia Collins	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9-14,16-22,24,36,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-14,16-22,24,36,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed March 25, 2002, paper no.10, has been entered.

Claims 5-8, 15, 23, 25-35 and 37 are cancelled.

Claims 1, 4, 16-20, 22, 24 and 36 are newly amended.

Claims 38-39 are newly added.

Claims 1-4, 9-14, 16-22, 24, 36 and 38-39 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

Figures 4 and 5 remain objected to because they are undecipherable. The figures appear to be black and white copies of color photographs. In the last office action, the submission of original color photographs was suggested to illustrate concepts such as "greening". Figures 4 and 5 as currently submitted are merely solid gray and black squares that do not illustrate anything. If Applicant does not wish to submit the original color photographs, Applicant is encouraged to cancel Figures 4 and 5, as well as their description in the specification.

Specification

The objection to the specification as not containing an abstract on a separate sheet is withdrawn in light of Applicant's submission of an abstract on a separate sheet.

Claim Rejections - 35 USC § 112

Claim 4 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention, for the reasons of record set forth for claims 4-6 in the office action mailed September 25, 2001.

Applicant's arguments filed March 25, 2002, have been fully considered but they are not persuasive.

Applicant points to page 10 of the specification which states that overexpressing betaine dehydrogenase and choline monooxygenase under a low temperature-induced promoter may allow the accumulation of betaine. Applicant asserts that one skilled in the art of plant transgenics would be familiar with the techniques involved in generating a plant that expresses a gene involved in betaine synthesis, and that the specification clearly demonstrates that increasing the concentration of betaine in a plant increases cold or freezing tolerance in a plant (reply page 6).

Applicant also argues that researchers have successfully increased the concentration of glycine betaine by metabolic engineering, and cites several examples from the prior art that demonstrate that overexpressing betaine dehydrogenase and choline monooxygenase can result in an increase in betaine. Applicant further argues that because the cited references of Rathinasabapathi et al. and Nuccio et al. relate to tobacco, which is not recited in the method of claim 1, these references do not provide a basis to object to amended claim 1 as lacking enablement (reply page 8).

The Examiner maintains that the mere assertion that overexpressing betaine dehydrogenase and choline monooxygenase under a low temperature-induced promoter may allow the accumulation of betaine does not enable the claimed invention, because overexpressing

betaine dehydrogenase or choline monooxygenase in a plant in a manner that results in accumulation of betaine sufficient to affect cold or freezing tolerance is unpredictable. Furthermore, while one skilled in the art of plant transgenics would be familiar with the techniques involved in generating a plant that expresses any gene, it would require undue experimentation for one skilled in the art to determine how to express a gene involved in betaine synthesis in a manner that results in accumulation of betaine sufficient to affect cold or freezing tolerance.

The Examiner does not generally question the enablement of the methods for increasing the concentration of glycine betaine by metabolic engineering disclosed in the prior art, but maintains that Applicant is not enabled for the claimed method because Applicant has not disclosed any method for increasing the concentration of glycine betaine by metabolic engineering. Furthermore, the Examiner maintains that the cited references of Rathinasabapathi et al. and Nuccio et al. provide a basis to question the enablement of any method for increasing the concentration of a biosynthetic product by metabolic engineering in any plant species, because the availability of substrates for heterologous enzymes introduced into any plant is unpredictable, and the subsequent fate of the product produced by the heterologous enzymes is also unpredictable.

Claims 1-3, 9-14, 16-22, 24 and 36 remain rejected, and claims 38-39 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing or inducing cold or freezing tolerance in the wheat cultivar Glenlea, said method comprising simultaneously acclimating the plant and increasing the concentration of betaine in

the plant by administering a betaine composition, wherein the lethal temperature of the plant is decreased, wherein the acclimation temperature is 6° C during the day and 2° C during the night, and wherein the betaine composition comprises betaine at 100 to 250 mM, does not reasonably provide enablement for other methods of increasing or inducing cold or freezing tolerance in other plants, for the reasons of record set forth in the office action mailed September 25, 2001.

Applicant's arguments filed March 25, 2002, have been fully considered but they are not persuasive.

Applicant argues that the application describes how the optimal betaine concentration can be established for several gramineae species. Applicant also points to several other reports that provide proof for Applicant's assertion that increased betaine levels can improve cold tolerance, and asserts that the effect of betaine accumulation in the plants recited in claim 1 is not highly unpredictable. Applicant argues that anyone skilled in the art could use the concentrations of betaine taught in the specification to establish the optimal concentration of betaine in new species by applying a range of concentrations (reply page 8).

Applicant further argues that the cited references do not provide a basis to object to amended claim 1 as lacking enablement because the cited reference of Gibon et al. relates to *Brassica*, and the cited reference of Xing et al. relates to *Arabidopsis*, whereas the method of amended claim 1 is directed to rosaceae species, gramineae species, and grass plants (reply page 9).

The Examiner maintains that the claimed invention is not directed to methods for determining optimal betaine concentration for different plant species, but to a method of

increasing or inducing cold or freezing tolerance in different plant species. Given the large number of plant species encompassed by the claims, and the variability of optimal betaine concentrations for different plant species, in the absence of further guidance or example it would require undue experimentation for one skilled in the art to determine what concentration of betaine to use in order to practice the claimed invention. Furthermore, while the Examiner does not generally question Applicant's assertion that increased betaine levels can improve cold tolerance, the Examiner maintains that the optimal betaine concentrations for the different plant species recited in claim 1 is unpredictable.

Furthermore, the Examiner maintains that the cited references of Gibon et al. and Xing et al. provide a basis to question the enablement of any method for increasing cold or freezing tolerance that requires increasing the concentration of betaine in different plant species, because the cited references teach that the optimal concentration of betaine varies between plant species. The Examiner further maintains that the teachings of Gibon et al. extend to plant species other than *Brassica* (see page 329 column 1 lines 18-22 and page 337 column 2 first full paragraph).

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "genes involved in the synthesis of betaine or a derivative thereof" is withdrawn in light of the amendment of claim 4.

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "one or more" is withdrawn in light of the amendment of claim 4.

The rejection of claim 18 under 35 U.S.C. 112, second paragraph, as being indefinite in the lack of antecedent basis for "composition" is withdrawn in light of the amendment of claim 18.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "overall physiology" and "at cold temperature" is withdrawn in light of the amendment of claim 24.

Claim 36 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "about an optimal cold or freezing tolerance", for the reasons of record set forth in the office action mailed September 25, 2001.

Applicant's arguments filed March 25, 2002, have been fully considered but they are not persuasive.

Applicant argues that amendment of the claim to recite "an optimal freezing tolerance" should overcome the rejection because the specification defines an optimal freezing tolerance as the temperature where fifty percent of the plant population die (LT_{50}) (reply page 9).

The Examiner maintains that while the specification discloses that the optimal freezing tolerance in the spring wheat variety Glenlea is expressed as the temperature where fifty percent of the plant population die (LT_{50}) (page 3 lines 20-23), the specification does not definitely define "optimal freezing tolerance" as the LT_{50}, as the claims are not limited to the spring wheat variety Glenlea.

Newly amended claims 1 and 24 and newly submitted claims 38-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly amended claims 1 and 24 and newly submitted claims 38-39 are indefinite in the recitation of "rosacea species", "gramineae species", "grass plant" or grasses. It is unclear what is intended by "grass plant" or "grasses" in this context, as "gramineae species" would ordinarily be considered to include grass plants and grasses.

Claim 1 is also indefinite in the recitation of "nontoxic concentration". It is unclear what concentration of betaine would be nontoxic in the context of the claimed method.

Claim Rejections - 35 USC § 103

Claims 1-3, 9-14, 16-20, 21-22, 24 and 36 remain rejected, and new claims 38-39 are rejected, under 35 U.S.C. 103(a) as being unpatentable over Rajashekar et al. (Plant Physiology, 1996, Vol. 111, No. 2 SUPPL., page 70) in view of Kishitani et al. (Plant, Cell, and Environment, 1994, Vol. 17, pages 89-95), and in light of Zhao et al. (Journal of Plant Physiology, 1992, Vol. 140, pages 541-543), for the reasons of record set forth in the office action mailed September 25, 2001.

Applicant's arguments as they apply to the currently rejected claims, filed March 25, 2002, have been fully considered but they are not persuasive.

Applicant argues that Rajashekar et al. fail to demonstrate that an increase in freezing tolerance is observed at the whole plant level. Applicant points out that Rajashekar et al. did not increase cold or freezing tolerance in strawberry plants, but only in the leaf organ, and thus does

not teach the successful induction of cold or freezing tolerance because the whole plant should be tolerant, not just the leaf. Applicant also argues that Rajashekar et al. fail to indicate the extent of increase in freezing tolerance, and do not show that the increase would surpass the genotypic capacity for cold and freezing tolerance. Applicant argues that it is impossible to predict from Rajashekar et al. that cold or freezing tolerance could be improved above the maximum achieved by cold acclimation alone or betaine application alone. Applicant asserts that an observation of increased tolerance at the leaf level is not indicative of a significant increase at the whole plant level. Applicant argues that Applicant's own independent tests revealed that 2mM betaine has no effect on the freezing tolerance of strawberry or other plant species (reply page 10).

Regarding the cited reference of Kishitani et al., Applicant argues that an observation of increased freezing tolerance at the leaf level is not indicative of a significant increase at the whole plant level. Applicant also argues that Kishitani et al. do not teach the combined treatment of exogenous betaine and cold acclimation in order to increase the level of freezing tolerance above the genetic capacity in barley (reply page 11).

Regarding the cited reference of Zhao et al., Applicant argues that Zhao et al. do not teach the combined treatment of exogenous betaine and cold acclimation in order to increase the level of freezing tolerance above the genetic capacity in alfalfa (reply page 11).

While Applicant asserts that an observation of increased cold or freezing tolerance at the leaf level is not indicative of a significant increase at the whole plant level, in the absence of evidence to the contrary, the Examiner maintains that increased cold or freezing tolerance at the

leaf level is indicative of a significant increase at the whole plant level, as the leaf is a significant portion of the whole plant in many plant species, and because the leaf is an organ that is ordinarily susceptible to the detrimental effects of cold or freezing temperatures. The Examiner also maintains that the combined treatment of exogenous betaine and cold acclimation would be expected to increase cold tolerance over the plant's normal genotypic potential, because one skilled in the art would recognize that the application of exogenous betaine would allow for accumulation of higher concentrations of betaine than the plant would be able to synthesize in response to cold acclimation alone, and because one skilled in the art would also recognize that many physiological changes other than betaine accumulation are known to occur as a consequence of cold acclimation. The Examiner further maintains that Applicant's mere assertion that Applicant's own independent tests revealed that 2mM betaine has no effect on the freezing tolerance of strawberry or other plant species is not sufficient to invalidate the cited reference of Rajashekar et al.

The rejection of claim 24 under 35 U.S.C. 103(a) as being unpatentable over Rajashekar et al. (Plant Physiology, 1996, Vol. 111, No. 2 SUPPL., page 70) in view of Virtanen et al. (WO 97/08951 13 March 1997), and in light of Kishitani et al. (Plant, Cell, and Environment, 1994, Vol. 17, pages 89-95), is withdrawn in light of the amendment of claim 24.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
August 10, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638